



CACNA1S gene

calcium voltage-gated channel subunit alpha1 S

Normal Function

The CACNA1S gene belongs to a family of genes that provide instructions for making calcium channels. These channels, which transport positively charged calcium atoms (ions) into cells, play a key role in a cell's ability to generate and transmit electrical signals.

The CACNA1S gene provides instructions for making calcium channels that are abundant in muscles used for movement (skeletal muscles). For the body to move normally, these muscles must tense (contract) and relax in a coordinated way. Muscle contractions are triggered by the flow of certain ions into muscle cells. Channels made with the CACNA1S protein control the transport of calcium ions into muscle cells and are part of the cellular machinery that initiates muscle contractions.

Channels made with the CACNA1S protein also activate a protein called ryanodine receptor 1 (produced by the *RYR1* gene). Ryanodine receptor 1 forms a channel that releases stored calcium ions within muscle cells in response to certain signals. The resulting increase in calcium ion concentration stimulates muscle fibers to contract, allowing the body to move.

Health Conditions Related to Genetic Changes

hypokalemic periodic paralysis

At least four mutations in the CACNA1S gene have been identified in people with hypokalemic periodic paralysis. These mutations cause up to 70 percent of all cases of this disorder.

Mutations in the CACNA1S gene change single protein building blocks (amino acids) used to make the CACNA1S protein, which alters the structure and function of calcium channels in skeletal muscle cells. The altered channels open more slowly than usual, reducing the flow of calcium ions into these cells. This disruption in calcium ion transport prevents muscles from contracting normally. It is unclear precisely how these changes lead to episodes of muscle weakness in people with hypokalemic periodic paralysis.

malignant hyperthermia

CACNA1S mutations account for a very small percentage of all cases of malignant hyperthermia. Researchers have identified two mutations in the CACNA1S gene

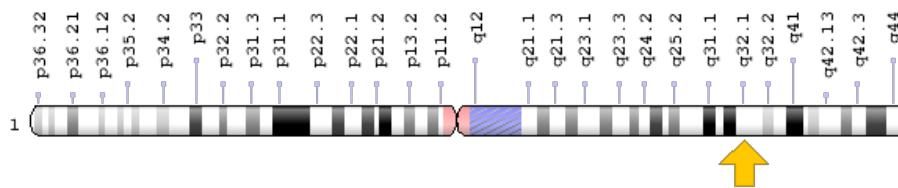
that are associated with an increased risk of this condition. One of these mutations replaces the amino acid arginine with the amino acid cysteine at protein position 1086 (written as Arg1086Cys); the other mutation replaces the amino acid arginine with the amino acid histidine at the same protein position (Arg1086His).

Genetic mutations likely cause channels made with the CACNA1S protein to activate the RYR1 channel improperly in response to certain drugs (particularly some anesthetics and a type of muscle relaxant used during surgery). As a result, large amounts of calcium ions are released from storage within muscle cells. An overabundance of available calcium ions causes skeletal muscles to contract abnormally, which leads to muscle rigidity in people with malignant hyperthermia. An increase in calcium ion concentration also activates processes that generate heat (leading to increased body temperature) and produce excess acid (leading to acidosis).

Chromosomal Location

Cytogenetic Location: 1q32.1, which is the long (q) arm of chromosome 1 at position 32.1

Molecular Location: base pairs 201,039,509 to 201,112,566 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CAC1S_HUMAN
- CACH1
- CACN1
- CACNL1A3
- calcium channel, voltage-dependent, L type, alpha 1S subunit
- Cav1.1
- CCHL1A3
- DHPR

- dihydropyridine receptor
- dihydropyridine-sensitive L-type calcium channel alpha-1 subunit
- HOKPP
- HypoKPP
- hypoPP
- MHS5
- Voltage-dependent L-type calcium channel subunit alpha-1S
- voltage-gated calcium channel subunit alpha Cav1.1

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Ca₂₊ channel mutations produce hypokalemic periodic paralysis
<https://www.ncbi.nlm.nih.gov/books/NBK28162/#A3041>
- Eurekah Bioscience Collection: High Voltage-Activated Ca₂₊ Channels
<https://www.ncbi.nlm.nih.gov/books/NBK6181/#A30865>
- Molecular Cell Biology (fourth edition, 2000): Muscle: A Specialized Contractile Machine
<https://www.ncbi.nlm.nih.gov/books/NBK21670/>
- Neuromuscular Disease Center, Washington University
<http://neuromuscular.wustl.edu/mother/chan.html#ca>

GeneReviews

- Hypokalemic Periodic Paralysis
<https://www.ncbi.nlm.nih.gov/books/NBK1338>
- Malignant Hyperthermia Susceptibility
<https://www.ncbi.nlm.nih.gov/books/NBK1146>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28CACNA1S%5BTIAB%5D%29+OR+%28CACNL1A3%5BTIAB%5D%29+OR+%28CCHL1A3%5BTIAB%5D%29+OR+%28dihydropyridine+receptor%5BTIAB%5D%29+OR+%28CACH1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- CALCIUM CHANNEL, VOLTAGE-DEPENDENT, L TYPE, ALPHA-1S SUBUNIT
<http://omim.org/entry/114208>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_CACNA1S.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=CACNA1S%5Bgene%5D>
- HGNC Gene Family: Calcium voltage-gated channel subunits
<http://www.genenames.org/cgi-bin/genefamilies/set/253>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=1397
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/779>
- UniProt
<http://www.uniprot.org/uniprot/Q13698>

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